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09/646,740	09/18/2000	Wolfgang Wuttke	WINTE-045244	5915

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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1651	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/646,740	Applicant(s) Wuttke et al.
	Examiner Michele Flood	Art Unit 1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 29, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-26* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on May 29, 2002. Acknowledgment is made of newly submitted Claim 26.

Claim 17-26 are under examination.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-26 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide prior support or antecedent basis for the language "*Belamcanda chinensis, Iris Germanica, Iris tectorum, Iris Illyrica, and Iris dichotoma*" in Claim 17.

The claims as set forth in the amendment filed May 29, 2002, now recite a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from an Iridaceae plant, wherein the plant extract is selected from the

group consisting of *Belamcanda chinensis, Iris germanica, Iris tectorum, Iris illyrica, and Iris dichotoma*. However, the specification as originally filed provides only for a method comprising the administration of a medicament comprising extracts obtained from *Belamcanda chinensis*.

Insertion of the above mentioned claim limitations have no support in the as-filed specification. The insertion of the limitations is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept for the claimed method for producing an estrogen-like effect in a patient without causing a substantial utereotrophic effect comprising the administration of a medicament comprising an extract obtained from the claimed Iridaceae plant specia. There is only one exemplified method for producing an estrogen-like effect in a patient without causing a substantial utereotrophic effect comprising the administration of a medicament comprising an extract obtained from *Belamcanda sinensis*. This is not sufficient support for the new genus, i.e., *Belamcanda chinensis, Iris Germanica, Iris tectorum, Iris illyrica, and Iris dichotoma*. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of the above mentioned claim limitations is considered to be the insertion of new matter for the above reasons.

As the above mentioned claim limitations could not be found in the present specification, the recitation of the claim limitations are deemed new matter; and, therefore they must be omitted from the claim language, unless Applicant can particularly point to the specification for literal support.

This is a new matter rejection.

Claims 17 and 19-26 as amended remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising administering to the patient an effective amount of *Belamcanda sinensis*, does not reasonably provide enablement for a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising administering to the patient an effective amount of a medicament comprising an extract from any of the plant members recited in the Markush group of Claim 17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Newly applied as necessitated by amendment.

The claims are drawn to a method of producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae plant, wherein the extract is selected from the group consisting of *Belamcanda chinensis, Iris germanica, Iris*

tectorum, Iris illyrica, and Iris dichotoma, and/or comprises at least of tectorigenin and tectorigenin glycoside, with the proviso that the medicament does not comprise *Belamcanda chinensis* extract if the medicament is used for treating a peri-menopausal or post-menopausal disorder.

The specification broadly discloses a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising the administration of the a claim-designated extract from Iridaceae plant, and tectorigenin and/or tectorigenin glycosides as a medicament. While the specification does demonstrate an *in vitro* method and an *in vivo* method for producing an estrogen-type effect in an ovariectomized rat (a recognized model for the post-menopausal woman in whom the endogenous estradiol production has subsided) comprising the single or repeated administration (i.e., organic solvents or with supercritical carbon dioxide*) Belamcanda sinensis* extract, wherein the claimed functional effect resulted in the lowering of serum LH levels, an inhibition of the GnRH pulse generator in hypothalamic estrogen-receptive structures, and inhibition of hyophysary LH secretion and similar functional effects comprising the administration of tectorigenin to ovariectomized rats, the specification does not disclose a method for producing an estrogen-type in patient without causing a substantial effect comprising the administration of an effective amount of a medicament comprising an extract obtained from any of the Iridaceae plants recited in Claim 17, namely *Belamcanda chinensis, Iris germanica, Iris tectorum, Iris illyrica, and Iris dichotoma*. There is no guidance in the specification, other than the aforementioned examples directed to the delivery

of either an extract of *Belamcanda sinsensis* or tectorigenin to ovariectomized rats. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effective amounts of extract intended for a therapeutic treatment for the claimed disease conditions. Moreover, as the claims are drawn to a method of administering pharmaceutically acceptable compositions which would in effect 'prevent' the various disease conditions from happening, they would require supporting evidence which clearly define the ingredients or constituents therein and supporting evidence because of the unpredictability in biological responses to therapeutic treatments or therapeutic prophylaxis. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effect or prophylactic effect, and describe the effective amounts of each ingredient for the administration of the composition intended for a therapeutic treatment or prophylaxis. Furthermore, the instant application does not provide a working example providing data which shows that the composition of the instant claims would indeed prevent an event such as the claimed designated disease conditions. Thus, Applicant has not demonstrated the claimed functional effect of preventing and treating each and every of the claimed disease conditions comprising the administration of plant extracts obtained from the aforementioned Iridaceae plants. Other than the demonstrated administration of the claimed medicaments comprising either an extract of *Belamcanda sinensis* and tectorigenin, Applicant has not demonstrated a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect method, said

method comprising administering to a patient an effective amount of the claim-designated plant extracts from the Family Iridaceae, with the proviso that *Belamcanda sinensis* extract is not used for treating peri-menopausal and post-menopausal disorders. Furthermore, it is noted that the specification is particularly silent as to which organic solvents are used in the making of the *Belamcanda sinensis* extract or from which plant source, if any plant source at all, the tectorigenin is obtained. Accordingly, it would take undue experimentation without a reasonable expectation of success as to how to determine the solvents used in the making of the claim designated plant extracts of the Family Iridaceae, how to determine the plant parts used in the making of the claimed designated plant extracts of the Family Iridaceae, and how to determine the effective therapeutic amounts of the claim designated plant extracts belonging to the Family Iridaceae which would have the claimed functional therapeutic effect in the treatment and/or prophylaxis of the claimed disease conditions, as broadly claimed by Applicant.

The Office further notes that while the amended claims have been rewritten to recite *Belamcanda chinensis,* throughout the specification Applicant recites *Belamcanda sinensis*. The lack of clarity as to the subject matter Applicant intends to direct the invention is deemed very confusing. It is not apparent from either the recitation of the amended claims or the specification whether or not the term "*Belamcanda sinensis*" is a typographical error. As the term "*Belamcanda sinensis*" was found unsearchable, it would appear that the recitation of the term throughout the specification fatally flaws the disclosure, if indeed the recitation of the term is not a typographical error.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-26 as amended remain/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Newly applied as necessitated by amendment.

Claim 17 is rended vague and indefinite by the phrase "an extract from an Iridaceae plant, wherein the extract" because the recited group members are plants and not extracts. The lack of clarity renders the claim ambiguous.

Claim 17 is rendered vague and indefinite by the phrase "and/or comprises at least of tectorigenin and tectorigenin glycoside" because it is unclear as to the subject matter Applicant intends to direct the invention. For instance, it is uncertain as to whether the phrase defines what is in the plant extract or whether Applicant intends to direct the invention to an alternative embodiment of the claimed invention that does not include the plant extracts or yet another embodiment of the claimed invention. If Applicant intends to direct the invention to another embodiment of the claimed invention comprising the use of a medicament or an extract, wherein the extract is obtained from any plant of the Family Iridaceae or any other plant extract, comprising "at least of tectorigenin and tectorigenin glycoside", the Office notes that Applicant

claims subject matter beyond the scope of the limitations originally presented and examined on the merits in the previous Office action.

Claim 26 is rendered vague and indefinite by the phrase "wherein the extract is produced with an organic solvent or supercritical CO_2" because the recitation of the phrase is generally narrative. For instance, it is uncertain as to how the extract is produced "with" an organic solvent or supercritical CO_2. Is the organic solvent or the supercritical CO_2 added to or combined with the claim-designated Iridaceae extract after the extract is obtained by an extraction process? The lack of clarity makes the claims ambiguous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 18, 24 and 26 as amended remain/are rejected under 35 U.S.C. 102(b) as being anticipated by JP 07138179A (N). Newly applied as necessitated by amendment. The rejection stands for the reasons set forth in the previous Office action and set forth below.

Applicant argues that JP 07138179A fails to anticipate the instantly claimed invention because JP 07138179A does not teach or suggest that the preparation produces an estrogen-type

effect in a patient without causing a substantial uterotrophic effect as disclosed by Applicant. However, Applicant's argument is not persuasive because JP 07138179A teaches the administration of a medicament comprising an extract of *Belamcanda chinensis*, which prevents skin ageing. The composition is obtained in an extraction method using water, lower alcohol or polyol organic solvent. The method of using the referenced composition is not expressly taught as a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect. However, the instantly claimed process is a one-step process of administering an effective amount of an extract obtained from *Belamcanda chinensis* to provide the claimed functional effect for the production of an estrogen-type effect for the treatment of a climacteric disorder. Thus, the functional effect of producing the estrogen-type effect in a patient without causing a substantial uterotrophic effect is inherent to the method of administering the *Belamcanda chinensis* composition taught by JP 07138179A, since the process steps and the ingredients used in the process steps are one and the same as disclosed by Applicant, since the referenced medicament is not expressly used for treating a peri-menopausal or post-menopausal disorder. As skin-ageing is known in the art as a climacteric disorder, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-26 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Esaki (U) and Petrie et al. (A) in view of Shawl (V) and Zhou et al. (W). Newly applied as necessitated by amendment.

Applicant's arguments have been fully considered but they are not deemed persuasive because the cited references provide the suggestions and motivation to the claimed invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching,

suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the primary reference of Esaki was relied upon because Esaki teaches that the administration of tectoridin (a tectorigenin glycoside) and tectorigenin to the rat causing a weak estrogen like action. The secondary reference of Petrie was relied upon because Petrie teaches the administration of representative compounds for the treatment and prophylaxis of various disease conditions, including age-related osteoporosis, in Column 4, lines 46-65. See Column 21, lines 58-61, wherein Petrie teaches the use of tectorigenin in the referenced method. Because neither Esaki nor Petri teach a method for producing an estrogen-type in a patient comprising the administration of a medicament comprising an extract obtained from the claim-designated plant extracts obtained from the Family Iridaceae the references of Shawl and Zhou were depended upon because Shawl teaches that both tectoridin and tectorigenin can be isolated from *Iris crocea* and Zhou teaches that both tectoridin and tectorigenin can be isolated from an ethanolic extract of the roots of *Belamcanda chinensis.*

Thus, with Esaki and Petrie providing the motivation to administer compositions comprising tectorigenin and tectoridin (a tectorigenin glycoside) for producing an estrogen-like effect in a patient without causing a substantial uterotrophic effect and for the treatment of the claim-designated disease conditions, and with Shawl providing plant extracts obtained from the family Iridaceae that comprise both tectoridin and tectorigenin, and finally with Zhou teaching

that both tectoridin and tectorigenin can be isolated from an ethanolic extract of the roots of *Belamcanda chinensis*, it would have been obvious to one of ordinary skill in the art to provide the claimed method because at the time the invention was made it was well known in the art that tectorigenin and tectorigenin glycoside could be obtained from a plant belonging to the family Iridaceae, as evidenced from the teachings of Shawl and Zhou. At the time the invention was made, one of ordinary skill in the art would have been motivated to provide a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, said method comprising the administering to a patient an effective amount of a medicament comprising an extract obtained from a plant of the Family Iridaceae, such as the referenced *Belamcanda chinensis* extract taught by Zhou, wherein the extract either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because both Shawl and Zhou teach plant extracts of the Family Iridaceae which comprise tectorigenin and tectorigenin. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to administer the claim designated plant extract taught by Zhou or to enrich the referenced Zhou extract with the tectorigenin and tectorigenin glycoside containing extracts taught by Shawl to provide the claimed functional effect and therapeutic effect for treatment and prophylaxis of various disease conditions, wherein the plant extracts either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because Esaki shows administering tectorigenin and tectoridin has estrogen like action with low toxicity and Petrie teaches that the administering of compounds of the general structure of tectorigenin

are effective in the treatment and prophylaxis of osteoporosis, age-related osteoporosis, post-menopausal osteoporosis, wound healing or tissue repair, elevation of peak bone mass in pre-menopausal women, arthritis, etc.

With regard to Claims 21-22 and 24-25, one of ordinary skill in the art would have been motivated to administer a plant extract from the family Iridaceae, plant extract either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because Petrie teaches an *in vivo* method for the administration of his compounds to ovariectomized animals, wherein the claimed functional effect of producing an estrogen-type effect with minimal uterotrophic effect is demonstrated (see Column 10, lines 51-67 to Column 11, lines 1-13). As it was well known in the art at the time the invention was made that ovariectomized animals are a model for the for the post-menopausal woman in whom the endogenous estradiol production has subsided, one of ordinary skill in the art would have had a reasonable expectation of success that the administering of the claim designated plant extracts from the family Iridaceae, wherein the plant extract comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside would have the claimed functional effect for being effective in each of the claim designated disease conditions because each of the claim designated disease conditions were associated with the menopausal woman.

As each of the references clearly indicate that the various proportions and amounts of the ingredients used in the claimed composition or the claimed composition/pharmaceutical

combinations are result variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by that reference.

Applicant's remarks with regard to the use of improper hindsight in the previous Office action have been noted but the references clearly show the claims rendered obvious for the reasons discussed above. The fact that Applicant has selected teachings from these references is still deemed obvious. At the time the invention was made the teachings of the references were clearly in the public domain and one of ordinary skill in the art would have known of these references and could have selected the teachings as Applicant appears to have done. Therefore, the invention as a whole was clearly prima facie obvious in the absence to the contrary.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. The examiner can normally be reached on Monday through Friday from 7:15 am to 3:45 pm. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Michael Wityshyn whose telephone number is (703) 308-4743.

MCF

July 31, 2002

CHRISTOPHER R. TATE
PRIMARY EXAMINER